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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N.	Applicant(s)
	09/345148	SEGAL
	Examiner	Art Unit
	GSMDEL	1644

-Th MAILING DATE of this communication appears on the cover sheet with th correspondence address -

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 4/5/01; 12/14/01

2a)☐ This action is **FINAL**. 2b)☑ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) ____ is/are pending in the application. 1-70

4a) Of the above claim(s) ____ is/are withdrawn from consideration. 15-16, 19, 20, 27, 30-68

5)☐ Claim(s) ____ is/are allowed.

6)☑ Claim(s) ____ is/are rejected. 1-14, 17-18, 21-25, 28, 29, 69-70

7)☐ Claim(s) ____ is/are objected to.

8)☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on ____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on ____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. ____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☑ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☑ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
4)☐ Interview Summary (PTO-413) Paper No(s). ____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's election of the species CD40-specific antibody, alpha chain of C3b and IL-2 in Paper No. 10, filed 4/5/01 and in Paper No. 13, filed 12/19/01.

Upon a review of the claims, claim 15 should have been placed in Group II and not Group I; therefore, claim 15 has been removed from the elected invention.

Upon a review of the claims, it appears that claims 17-18 and 21-26 should be in Group I as well.

Therefore, Group I includes claims 1-14, 17-26, 28, 29 and 69-70.

Claims 1-14, 17-18, 21-25, 28, 29 and 69-70 are being acted upon as the elected invention

As pointed out in the rejection under 35 USC 112, second paragraph, below, the claims are ambiguous as to the nature and metes and bounds of the "CD40 ligand enhanced cell and "engineered ligand for CD40, particularly as it reads on the elected invention. Applicant is invited to amend the claims to distinctly recite the claimed invention, particularly as it reads on the elected invention.

Claims 15-16, 19, 20, 27 and 30-68 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected inventions and/or species.

2. Applicant should amend the first line of the specification to provide for the priority documents. For example, the first line of the specification does not claim the benefit of U.S. Provisional Application No. 60/091,525, filed 7/2/98. See MPEP 1302.04

3. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

4. Claims 1-14, 17-18, 21-25, 28, 29 and 69-70 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are indefinite in the recitation of "CD40 ligand enhanced cell and "engineered ligand for CD40, particularly in light of the elected invention of CD40-specific antibody because the nature as well as the metes and bounds of "CD40 ligand enhanced cell" and "engineered ligand for CD40" are ambiguous and unclear.

For example, it is not clear whether the "CD40 ligand (CD40-specific antibody)" is incorporated into or onto the cell or provided as a separate element of a composition.

Also, the metes and bounds of an engineered ligand for CD40, particularly as it reads on CD40-specific antibody, are ambiguous. For example, does an engineered ligand for CD40 read on any antibody or on particular types of antibodies such as monoclonal antibodies, chimeric antibodies or humanized antibodies ?

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

5. Given the broadest interpretation of the claimed invention, particularly in light of the elected invention of CD40-specific antibody and the recitation of "admixed with an engineered ligand for CD40", the instant methods are interpreted to include a mixture of cell comprising an antigen and mixed with a CD40-specific antibody.

Given the recitation of the dependent claims wherein the ligand for CD40 comprise a lipid, including a GPI moiety; the elected invention appears to include the CD40-specific antibody attached to the cell as well as a separate element in a composition mixture.

Also, it is noted that the elected invention is CD40-specific antibody. However, given the applicability of a reference in the obviousness rejection under 35 USC 103(a), the reference has been applied under 35 USC 102(e) as well given the breadth of the claimed invention.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined *under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e))*.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 2, 5-9 and 15 are rejected under 35 U.S.C. § 102(e) as being anticipated by Maraskovsky et al. (U.S. Patent No. 6,017,527) (see entire document).

Maraskovsky et al. teach the methods of vaccination with antigen-expressing activated dendritic cells, including stimulating immune responses with the administration of other cytokines such as the CD40 ligand and IL-2 (e.g. see column 6, paragraph 1; column 11, paragraph 4). Here, transfecting the dendritic cells to express the cytokines is also taught. The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113. Such CD40 ligand and IL-2 cytokines would be engineered or recombinantly made.

Maraskovsky et al. teach antigens from a number of pathogenic organisms encompassed by the claimed invention, including bacteria, virus tumor associated antigens (see Preparation of Antigens on columns 10-11).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to vaccinate with antigen-expressing activated dendritic cells with CD40 ligand and/or IL-2 separately or co-transfected to various pathogenic organisms.

9. Claims 1, 2, 5-9 and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Maraskovsky et al. (U.S. Patent No. 6,017,527) in view of (Dullforce et al. (Nature Medicine 4: 88-91, 1998; 1449) AND/OR Heath et al. (Eur. J. Immunol., 24: 1828-1834, 1994) AND/OR and Caux et al. (Research in Immunology 145: 235-239, 1994).

Maraskovsky et al. teach the methods of vaccination with antigen-expressing activated dendritic cells, including stimulating immune responses with the administration of other cytokines such as the CD40 ligand and IL-2 (see entire document, including column 6, paragraph 1; column 11, paragraph 4). Here, transfecting the dendritic cells to express the cytokines is also taught.

Maraskovsky et al. teach antigens from a number of pathogenic organisms encompassed by the claimed invention, including bacteria, virus tumor associated antigens (see Preparation of Antigens on columns 10-11).

It is noted that Maraskovsky et al. teach that anti-CD40 antibodies have been shown to mediate various biological activities (see column 7, lines 61-65). However, Maraskovsky et al. differs from the claimed methods by not disclosing the administration of agonistic CD40-specific antibodies per se.

Dullforce et al. teach the administration of agonistic CD40-specific antibodies as adjuvants to stimulate B cells and antigen presenting cells against bacterial pathogens (see entire document, including Abstract). While Dullforce et al. focus on T cell-independent immune responses, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the administration of known agonistic anti-CD40 antibodies would have been applicable to various pathogenic organisms and antigens. It is noted that anti-CD40 antibodies stimulate antigen presenting cells and that human B cells are antigen presenting cells.

Heath et al. teach anti-CD40 antibodies, including various epitopic specificities, that are capable of stimulating immune responses such as B cells as well as the use of such antibodies in infectious diseases and malignancy (page 1833, column 2) (see entire document, including Abstract and Discussion).

Caux et al. teach the expression of functional CD40 on B lymphocytes and dendritic cells (see entire document).

Given the teachings of Maraskovsky et al. of employing stimulation immune responses via the CD40 pathway, it would have been obvious to one of ordinary skill in the art to employ the known agonistic anti-CD40 antibodies, taught by Heath et al. and Caux et al., in the methods of vaccinating with antigen-expressing activated dendritic cells, taught by Maraskovsky et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to select agonistic CD40 antibodies to stimulate immune responses via CD40 expressing antigen presenting cells to increase the immune response to antigen expressing dendritic cells to a variety of pathogenic organisms. As pointed out above, Maraskovsky et al. teach combining antigen expressing activated dendritic cells with other reagents that costimulate immune responses (see column 11, paragraph 4). In addition to the teachings of agonistic CD40-specific antibodies, taught by Dullforce et al., heath et al. And Caux et al., it was well known and practiced at the time the invention was made to generate recombinant antibodies such as chimeric antibodies, humanized antibodies and fragments thereof to decrease immunogenicity and increase half-life of such recombinant antibodies. Therefore, the engineered CD40-specific antibodies encompassed the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made. The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113. Such anti-CD40 antibodies would comprise the idiotypic portion of an antibody which binds CD40.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

10. Claims 1, 2, 5-14, 17-18, 21-25, 28, 29 and 69 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Maraskovsky et al. (U.S. Patent No. 6,017,527) in view of Dullforce et al. (Nature Medicine 4: 88-91, 1998; 1449) AND/OR Heath et al. (Eur. J. Immunol., 24: 1828-1834, 1994) AND/OR and Caux et al. (Research in Immunology 145: 235-239, 1994).
as applied to claims 1, 2, 5-9 and 15 above and further in view of the well known use of engineering attachment of a lipid such as a long-chain fatty acid to a molecule such as a peptide to permit the complex to stably associated with the plasma membrane , including the use of palmitate as acknowledged on pages 64- 67 of the instant specification (see Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid), including the teachings of McHugh et al. (PNAS 92: 8059-8063, 1995)

The teachings of Maraskovsky et al. in view of Dullforce et al. AND/OR Heath et al. AND/OR and Caux et al. Have been set forth above and differ from the claimed methods as they read on methods of employing lipid linked anti-CD40 antibodies, encompassed by the breadth of the claims.

Pages 64- 67 of the instant specification (see Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid) provide for a number of teachings that acknowledge the well known use of engineering attachment of a lipid such as a long-chain fatty acid to a molecule such as a peptide to permit the complex to stably associated with the plasma membrane , including the use of palmitate.

Given that co-stimulatory nature of the CD40:CD40 ligand pathway and the co-stimulatory signal provided by anti-CD40 antibodies, the teachings of McHugh et al. are particularly relevant to the instant invention.

In exemplifying potent immune responses to tumor cells, McHugh et al. teach the use introducing costimulatory molecules into membranes via glycosyl-phosphatidylinositol (GPI) as an alternative approach to provide costimulatory molecules to stimulate immune responses of interests (see entire document, including page 8059, column 2, paragraphs 2-3, Materials and Methods, Results and Discussion). McHugh et al. teach that this eliminates the introduction of foreign DNA for tumor immunotherapy, for example, (see Introduction and Discussion). McHugh et al. teach combinations of costimulatory signals to create the optimal target to facilitate many T cell regulatory and effector functions (see page 8063, column 1, paragraph 3).

Again, McHugh et al. focus on tumor immunity, but one of ordinary skill in the art would have been motivated to employ GPI anchored co-stimulatory molecules with immunogenic cells to stimulate immune responses of interest.

Given the teachings and advantages of combining co-stimulatory molecules via alternative methods as taught by the above-mentioned references, one of ordinary skill in the art at the time the invention was made would have been motivated to modify antigen presenting dendritic cells with GPI anchored agonistic antibodies to increase stimulation to pathogenic organisms.

Alternative methods of producing a lipid-linked engineered anti-CD40 antibodies or cytokines by chemically linked the polypeptide to a fatty acid such as palmitate is also acknowledged by the instant specification (see Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid, particularly page 67, paragraph 2).

Further, given the teachings of Maraskovsky et al. of vaccinating for tumor antigens, including the use of CD40:CD40 ligand pathway and IL-2 (see above) and the teachings of McHugh et al. for teaching the provision of co-stimulatory signals in conjunction with tumor cell vaccination, the ordinary artisan would have been motivated at the time the invention was made to combine the co-stimulatory signal of anti-CD40 antibodies, taught by Dullforce et al., Caux and Heath, in conjunction with the tumor cells themselves to vaccinate against tumor cells and/or antigens of interest. It would have been immediately apparent to one of ordinary skill in the art that tumor cells would have been attentuated so that tumor cells would not be able to divide and proliferate in a host. If not, the tumor cells could proliferate to the point of being detrimental to the subject fo the vaccination.

Therefore, one of ordinary skill in the art would have been motivated to select agonistic CD40 antibodies to stimulate immune responses via CD40 expressing antigen presenting cells and/or tumor cells via GPI, as taught by McHugh et al., to increase the immune response to antigen expressing dendritic cells and/or tumor cells to a variety of pathogenic organisms, including tumor antigens as well as the those antigens encompassed by the bacteria, fungi and parasites. As pointed out above, Maraskovsky et al. teach combining antigen expressing activated dendritic cells with other reagents that costimulate immune responses (see column 11, paragraph 4).

In addition to the teachings of agonistic CD40-specific antibodies, taught by Dullforce et al., Heath et al. and Caux et al., it was well known and practiced at the time the invention was made to generate recombinant antibodies such as chimeric antibodies, humanized antibodies and fragments thereof to decrease immunogenicity and increase half-life of such recombinant antibodies. Such anti-CD40 antibodies would comprise the idiotypic portion of an antibody which binds CD40. Given the well known use and practice of recombinant technology to produce homogeneous proteins at the time the invention was made, engineered CD40-specific antibodies as well as engineered cytokines encompassed by the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made. The patentability of a product does not depend on its method of production. In re Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See MPEP 2113.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. Claims 3, 4 and 70 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Maraskovsky et al. (U.S. Patent No. 6,017,527) in view of Dullforce et al. (Nature Medicine 4: 88-91, 1998; 1449) AND/OR Heath et al. (Eur. J. Immunol., 24: 1828-1834, 1994) AND/OR and Caux et al. (Research in Immunology 145: 235-239, 1994).
as applied to claims 1, 2, 5-14, 17-18, 21-25, 28, 29 and 69 above and further in view of
and in further view of the known use of engineering attachment of a lipid such as a long-chain fatty acid to a molecule such as a peptide to permit the complex to stably associated with the plasma membrane , including the use of palmitate as acknowledged on pages 64- 67 of the instant specification (see Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid).McHugh et al. (PNAS 92: 8059-8063, 1995)
and further in view of Jacquier-Sarlin et al. (Immunology 84: 164-170, 1995).

Maraskovsky et al. in view of Dullforce et al. AND/OR Heath et al. AND/OR and Caux et al. further in Engineered Opsonins, Cytokines or Ligands for CD40 Containing a Lipid on pages 64-67 of the instant specification, including the teachings of McHugh et al differs from the claimed invention by not teaching the addition of the alpha chain of C3b.

Jacquier-Sarlin et al. teach the use of complement fragments including C3b to enhance immune responses to antigens of interest (see entire document). By increasing antigen processing and presentation, C3b could be engineered into new vaccines (see Discussion, particularly the last paragraph on page 169).

Given the teachings of Jacquier-Sarlin et al. that C3b which would include the alpha chain of C3b, increases antigen processing and presentation which would be useful for engineering vaccines, one of ordinary skill in the art would have been motivated to incorporate C3b into vaccine preparations to a host of pathogenic organisms and antigens, including tumor antigens in order to increase immunogenicity and, in turn, increase immune responses to antigens of interest.

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Jacquier-Sarlin to incorporate C3b into the methods of vaccination via alternative modes of compositions comprising immunogenic cells, anti-CD40 antibodies and IL-2, as taught above to obtain vaccination by a highly immunogenic composition to pathogenic organisms of interest, including tumor cells. The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combine for their common known purpose, which is increasing immunogenicity in methods of vaccination in the instant case. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
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November 4, 2002